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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,116	11/20/2001	John H. Healey	9958-004-999	6037

20583 7590 12/08/2003

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EXAMINER	
JAGOE, DONNA A	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,116	HEALEY ET AL.0	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claims 38-76 are pending in this application.

Response to Arguments

Applicant's arguments with respect to claims 1-36 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 38-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anuta U.S. Patent No. 4,341,691 and Lehtinen U.S. Patent No. 5,733,564 A. in view of Remington's Pharmaceutical Sciences

The claims are drawn to a composition comprising a polymeric bone cement in the form of particles and an anti-resorptive agent in the form of particles wherein the anti-resorptive agent's particle-size distribution is about the same as the polymeric bone-cement component's particle size distribution with dependent claims drawn to bisphosphonates, cholesterol lowering agents, estrogen-bisphosphonate conjugates and gallium as anti-resorptive agents and particle size's of 75 to 70 % with an average diameter of about 25 microns and about 30 to 35 % with an average diameter of about 13 to 17 microns.

Lehtinen et al teach bisphosphonate added to solution used for preservation of endo-osteal materials such as artificial joints, hip prostheses, dental and other implants (column 2, lines 25-36). Lehtinen teaches that bisphosphonate's main effect is their ability to inhibit bone resorption (column 3, lines 21-23). As an example, clodronate (a bisphosphonate) is employed to treat tibias, which were then more quickly and more extensively vascularized than the control tibias. It does not teach zoledronate, pamidronate, etidronate or alendronate. It would have been made obvious to one of ordinary skill in art at the time it was made to substitute zoledronate, pamidronate,

etidronate or alendronate for the clodronate of the prior art. It is prima facie obvious to substitute equivalents, motivated by the reasonable expectation that the respective species will behave in a comparable manner or give comparable results in comparable circumstances. *In re Ruff* 118 USPQ 343; *In re Jezel* 158 USPQ 99; the express suggestion to substitute one equivalent for another need not be present to render the substitution obvious. *In re Font*, 213 USPQ 532. It does not teach particle size as recited in dependent claims 50 and 51. Anuta teaches that the poly methyl methacrylate powder in Zimmers standard bone cement is comprised of a mixture of 65 to 70% polymer beads with a maximum average size of 25 microns and 30 to 35% of the beads have been milled (column 5, lines 43-47) and a bead fraction where the bead powder is sifted to a size range of 13 to 17 microns (column 6, lines 59-63). It would have been made obvious to one of ordinary skill in art at the time it was made to employ the recited particle sizes motivated by the recitation of Anuta that Zimmer's standard bone cement employs a mixture of 65 to 70% polymer beads with a maximum average size of 25 microns and 30 to 35% of the beads have been milled (column 5, lines 43-47) and a bead fraction where the bead powder is sifted to a size range of 13 to 17 microns (column 6, lines 59-63). Regarding applicant's remarks that when the particle size of the cement is about the same as the particle-size distribution of the anti-resorptive agent surprisingly prevents clumping and promotes even distribution of the anti-resorptive agent in the composition, Remington's Pharmaceutical Sciences, teaches that, in mixing powders, a large difference in particle size would tend to cause demixing (page 1570 1st full paragraph). Thus, when the particle sizes are similar, the powders

would tend to stay mixed. It would have been made obvious to one of ordinary skill in art at the time it was made to employ similar particle sizes of different agents motivated by the teaching of Remington's Pharmaceutical Sciences that a large difference in particle size would tend to cause demixing of a composition of powders.

2. Claims 54-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mao et al. U.S. Patent No. 6,238,687 B1 and Gayer et al. U.S. Patent No. 6,214,049 B1.

The claims are drawn to compositions comprising bone cement selected from organic, inorganic and composite combined with an anti-resorptive agent.

Mao et al. teach polymeric materials that can be used to produce surgical devices such as molded appliances (column 7, lines 4-12). The polymers can be used in a composition containing an active substance and can be used to produce a bone cement for repairing injury to bone (column 21, lines 10-16). The other active agents that can be added to the bone cement are anti-neoplastics, estrogenic substances, cholesterol-lowering agents such as cholestyramine, and gallium nitrate and titanium compounds (column 22. line 4 to column 23, line 17). It does not teach the bisphosphonates that are instantly claimed.

Gayer et al. teach moldable polymer matrix systems (column 3, lines 43-14) for bone replacement. The polymer may contain hydroxyapatite (column 10, lines 27-31) and osteoconductive factors such as bisphosphonate (column 11, lines 34-38). It does not recite the specific bisphosphonate agents instantly recited. It would have been

made obvious to one of ordinary skill in art at the time it was made to substitute zoledronate, pamidronate, etidronate or alendronate for the bisphosphonate of the prior art. It is prima facie obvious to substitute equivalents, motivated by the reasonable expectation that the respective species will behave in a comparable manner or give comparable results in comparable circumstances. *In re Ruff* 118 USPQ 343; *In re Jezel* 158 USPQ 99; the express suggestion to substitute one equivalent for another need not be present to render the substitution obvious. *In re Font*, 213 USPQ 532.

Regarding the specific concentrations recited, as anyone of ordinary skill in the art will appreciate, preferred concentrations are merely exemplary and serve as useful guideposts for the practitioner. There are, however, many reasons for varying the concentration, including by orders of magnitude; for instance, an older patient with osteoporosis or one having an unusually severe break/fracture would require a correspondingly higher concentration. Furthermore, it is routine during animal and clinical studies to dramatically vary dosage to obtain data on parameters such as toxicity. For these and other self-evident reasons, it would have been obvious to have used the doses of bisphosphonate recited instantly.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (703) 306-5826. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3230.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Donna Jagoe
Patent Examiner
Art Unit 1614

Frederick Krass
Primary Examiner
Art Unit 1614